

WHAT IS CLAIMED IS:

SUB
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1. A recombinant vector, pDATH-X (Dominant negative, Antisense, TET-ON controllable Heat shock promoter plasmid), said
5 vector comprising the cassettes:

(a) a fusion of the coding sequences for amino acids 1 -
207 of the tetracycline repressor and the C-terminus last 130 amino
acid transcription activation domain of the VP16 protein of the herpes
simplex virus;

10 (b) a heat shock promoter consisting of heat shock
response elements (-260 to 30) of the human heat shock 70 gene
promoter linked to the minimal cytomegalovirus promoter, pCMV;

(c) a tet operator consisting of the 19 bp inverted repeats
of the operator O2 of TN10 to which the tet repressor and TAKON bind;

15 and

(d) an antisense sequence consisting of the
complementary sequence to the first 80 bases of the TAKON sequence
including the ATG.

SUB
R2 2. A method of achieving sustained expression of a gene
under control of a heat or light inducible promoter, comprising the step
of:

introducing the vector containing said gene into the host
5 organism; and
applying heat or light energy.

3. The method of claim 2 where said host organism is a
10 human.

4. A recombinant vector, pDATE-X (Dominant negative,
Antisense, TET-ON controllable EGR promoter expression plasmid), said
15 vector comprising the cassettes:

(a) cassette 1 comprising the TET-ON sequence under the
control of the EGRp, the tetracycline operator binding site and pCMV;

(b) cassette 2 comprising a therapeutic gene X under the
control of the tetp-pCMV promoter;

(c) cassette 3 comprising antisense TET-ON under the control of the pCMV promoter; and

(d) cassette 4 comprising dominant negative TET-ON under the control of the pCMV promoter.

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5. A recombinant vector, pRIBs-X, (Radiation-Inducible, Breast-specific Promoter) expression vector, said vector comprising the cassettes:

(a) cassette 1 comprising "Gal-DBD-mx" which is a fusion open reading frame encoding the N-terminus (amino acids 1-147) DNA-binding domain of the yeast GAL4 protein (Gal-DBD) fused to the basic helix-loop-helix-leucine zipper domain of Max (amino acids 8-112) followed by SV40 poly A, wherein the resulting fusion gene GAL-DBD-mx is controlled by the radiation inducible Egr-1 promoter;

(b) cassette 2 comprising the minimal CMV promoter, "antisense Gal-DBD-mx", which is an antisense construct complementary to the Gal-DBD-mx sequence, an internal ribosomal entry site (IRES) and "Gal-DBD" which competes with the Gal-DBD-mx for the pGAL binding site;

5 (c) cassette 3 comprising "VP16-TA-mc" which is a fusion ORF encoding at the N-terminus the first 11 amino acids of Gal4 (amino acids 1-147), followed by the nuclear localization signal of the SV40 large T antigen, the 130 amino acid C-terminus transactivation domain of the herpes simplex viral protein VP16, the basic helix-loop-helix-leucine zipper domain of c-Myc (amino acids 350-439), followed by SV40 polyA, wherein the resulting fusion gene, VP16-TA-mc, is under the control of the c-erbB2 promoter "perB2" up to the first ATG;

10 (d) cassette 4 comprising "Galp", five copies of a 17-mer DNA-binding site for Gal4, wherein a TET-ON sequence is placed under the control of the GAPp-ptet promoter and a therapeutic gene X is linked to the TET-IN via an IRES;

15 (e) cassette comprising an antisense TET-ON which is a sequence consisting of the complementary sequence to the first 80 bases of the TET-ON sequence including the ATG under the control of the pCMV promoter; and

(f) cassette 6 comprising a dominant negative TET-ON consisting of the coding sequences for amino acids 1-207

6. The recombinant vector of claim 5, wherein the perbB2 promoter of cassette 3 is replaced with the whey acidic protein promoter.

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7. The recombinant vector of claim 5, wherein the perbB2 promoter of cassette 3 is replaced with the stromelysin 3 promoter.

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8. The recombinant vector of claim 5, wherein said gene X is a gene encoding tumor necrosis factor alpha.

9. A method of treating local and metastatic breast and ovarian cancer comprising the step of:

administering the expression vector of claim 5 to an individual in need of such treatment.

10. A method of treating local and metastatic breast and ovarian cancer comprising the step of:

administering the expression vector of claim 6 to an individual in need of such treatment.

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11. A method of treating local and metastatic breast and ovarian cancer comprising the step of:

administering the expression vector of claim 7 to an individual in need of such treatment.

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12. A recombinant pRIPs-X (Radiation-Inducible, Prostate-specific Promoter) expression vector, said vector comprising the cassettes:

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(a) cassette 1 comprising "Gal-DBD-mx" which is a fusion open reading frame encoding the N-terminus (amino acids 1-147) DNA-binding domain of the yeast GAL4 protein fused to the basic helix-loop-helix leucine zipper domain of Max (amino acids 8-112) followed by

SV40 polyA, wherein the resulting fusion gene GAL-DBD-mx is controlled by the radiation inducible Egr-1 promoter;

(b) cassette 2 comprising the minimal CMV promoter, antisense Gal-DBD-mx, which is an antisense construct complementary to the Gal-DBD-mx sequence, IRES, which is an internal ribosomal entry site and Gal-DBD which competes with the Gal-DBD-mx for the pGAL binding site;

(c) cassette 3 comprising "VP16-TA-mc", a fusion open reading frame encoding at the N-terminus the first 11 amino acids of Gal4, followed by the nuclear localization signal of the SV40 large T antigen, the 130 amino acid C-terminus transactivation domain of the herpes simplex viral protein VP16, the basic helix-loop-helix leucine zipper domain of c-Myc (amino acids 350-439), followed by SV40 polyA, wherein the resulting fusion gene, VP16-TA-mc, is under the control of the probasin gene promoter "pProbasin" up to the first ATG;

(d) cassette 4 comprising GALp, five copies of the 17-mer DNA-binding site for Gal4, wherein the TET-ON sequence is under the control of the GALp-ptet promoter and a therapeutic gene X is linked to the TET-ON via an internal ribosomal entry site;

(e) cassette 5 comprising an antisense TET-ON which is a sequence consisting of the complementary sequence to the first 80 bases of the TET-ON sequence including the ATG, under the control of the pCMV promoter; and

(f) cassette 6 comprising a dominant negative TET-ON consisting of the coding sequence for amino acids 1-207.

13. The recombinant vector of claim 12, wherein said probasin promoter of cassette 3 is replaced with the prostate specific antigen promoter.

14. The recombinant vector of claim 12, wherein said gene X is tumor necrosis factor alpha.

15. A method of treating local and metastatic prostate cancer comprising the step of:

administering the expression vector of claim 12 to an individual in need of such treatment.

16. A method of treating local and metastatic prostate cancer comprising the step of:

administering the expression vector of claim 13 to an individual in need of such treatment.

17. A recombinant expression vector, pHIBs-X (Heat Inducible, Breast-specific promoter), said vector comprising the cassettes:

(a) cassette 1 comprising Gal-DBD-mx which is a fusion open reading frame encoding the N-terminus (amino acids 1-147) DNA-binding domain of the yeast GAL4 protein fused to the basic helix-loop-helix leucine zipper domain of Max (amino acids 8-112) followed by SV40 polyA, wherein the resulting fusion gene GAL-DBD-mx is controlled by the heat inducible heat shock protein promoter;

(b) cassette 2 comprising the minimal CMV promoter, antisense Gal-DBD-mx, a construct complementary to the Gal-DBD-mx sequence, an internal ribosomal entry site and Gal-DBD, which competes with the Gal-DBD-mx for the pGAL binding site;

5 (c) cassette 3 comprising "VP16-TA-mc" which is a fusion open reading frame encoding at the N-terminus the first 11 amino acids (amino acids 1-147), followed by the nuclear localization signal of the SV40 large T antigen, the 130 amino acid C-terminus transactivation domain of the herpes simplex viral protein VP16, the basic helix-loop-helix leucine zipper domain of c-Myc (amino acids 350-439), followed by SV40 polyA, wherein the resulting fusion gene VP16-TA-mc is under the control of the c-erbB2 gene promoter "perbB2" up to the first ATG;

10 (d) cassette 4 contains GALp, five copies of a 17-mer DNA-binding site for Gal4, wherein the TET-ON sequence is under the control of the GALp-ptet promoter and a therapeutic gene, X, is linked to the TET-ON via an internal ribosomal entry site;

15 (e) cassette 5 comprising an antisense TET-ON which is a sequence consisting of the complementary sequence to the first 80 bases of the TET-ON sequence including the ATG, under the control of the pCMV promoter; and

(f) cassette 6 comprising a dominant negative TET-ON consisting of the coding sequences for amino acids 1-207.

18. The recombinant vector of claim 17, wherein the perbB2 promoter of cassette 3 is replaced with the whey acidic protein promoter.

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19. The recombinant vector of claim 17, wherein the perbB2 promoter of cassette 3 is replaced with the stromelysin 3 promoter.

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20. The method of claim 17, wherein said therapeutic gene is tumor necrosis factor alpha.

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21. A method of treating local and metastatic breast and ovarian cancer comprising the step of:

administering the expression vector of claim 17 to an individual in need of such treatment.

22. A method of treating local and metastatic breast and ovarian cancer comprising the step of:

administering the expression vector of claim 18 to an individual in need of such treatment.

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23. A method of treating local and metastatic breast and ovarian cancer comprising the step of:

administering the expression vector of claim 19 to an individual in need of such treatment.

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24. A recombinant vector, pHIPs-X (Heat-Inducible, Prostate-specific Promoter), said vector comprising the cassettes:

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(a) cassette 1 comprising Gal-DBD-mx which is a fusion open reading frame encoding the N-terminus (amino acids 1-147) DNA-binding domain of the yeast GAL4 protein fused to the basic helix-loop-helix leucine zipper domain of Max (amino acids 8-112) followed by SV40 polyA, wherein the resulting fusion gene GAL-DBD-mx is controlled by the heat inducible heat shock protein promoter;

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(b) cassette 2 comprising the minimal CMV promoter (mCMVp), antisense Gal-DBD-mx, a construct complementary to the Gal-DBD-mx sequence, an internal ribosomal entry site and Gal-DBD, which competes with the Gal-DBD-mx for the pGAL binding site;

5 (c) cassette 3 comprising "VP16-TA-mc", a fusion open reading frame encoding at the N-terminus the first 11 amino acids of Gal4, followed by the nuclear localization signal of the SV40 large T antigen, the 130 amino acid C-terminus transactivation domain of the herpes simplex viral protein VP16, the basic helix-loop-helix leucine
10 zipper domain of c-Myc (amino acids 350-439), followed by SV40 polyA, wherein the resulting fusion gene, VP16-TA-mc, is under the control of the probasin gene promoter "pProbasin" up to the first ATG;

(d) cassette 4 comprising GALp, five copies of a 17-mer DNA-binding site for Gal4, wherein the TET-ON sequence is under the
15 control of the GALp-ptet promoter and a therapeutic gene, X, is linked to the TET-ON via an internal ribosomal entry site;

(e) cassette 5 comprising an antisense TET-ON which is a sequence consisting of the complementary sequence to the first 80 bases of the TET-ON sequence including the ATG, under the control of
20 the pCMV promoter; and

(f) cassette 6 comprising a dominant negative TET-ON consisting of the coding sequences for amino acids 1-207.

25. The recombinant vector in claim 24, wherein the probasin promoter is replaced with the prostate-specific antigen promoter.

26. The recombinant vector of claim 24, wherein said therapeutic gene is tumor necrosis alpha.

27. A method of treating local and metastatic prostate cancer comprising the step of:

administering the expression vector of claim 24 to an individual in need of such treatment.

28. A method of treating local and metastatic prostate cancer comprising the step of:

administering the expression vector of claim 25 to an individual in need of such treatment.